tissues, the fœtal membranes of several species can utilize fructose almost as readily as glucose. Therefore, the possibility remains that the fructose of fœtal ungulates, which have unusually low blood glucose concentrations[4], may provide a source of energy for the amnion and allantois.

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PHARMACOLOGY

Effect of Drugs on the Uptake and Release of ^{3}H-Norepinephrine in the Rat Heart

FOLLOWING the administration of a wide variety of drugs such as psychoactive agents (reserpine, chlorpromazine, imipramine), sympathomimetic amines (tyramine, amphetamine), cocaine, adrenergic blocking agents (phenoxybenzamine), and hypotensive drugs (guanethidine) a lower concentration of injected ^{3}H-noradrenaline was found in the heart, spleen and adrenal glands[1–3]. Most of these drugs also increase the rate of metabolism of ^{3}H-noradrenaline in the whole mouse presumably by preventing the protective binding of the hormone and exposing it to enzymatic attack[4,5]. Although these drugs have many actions, they could produce a common-end result by different mechanisms. They might lower the tissue levels of ^{3}H-noradrenaline by blocking the entry of the circulating catecholamine into the storage site, preventing the binding or causing the release of the bound ^{3}H-noradrenaline or by a combination of these.

If a drug prevents the uptake, it should lower the tissue levels of ^{3}H-noradrenaline only when given before the ^{3}H-catecholamine. If it reduces the concentration when given after ^{3}H-noradrenaline when the hormone is bound in tissues, then it releases the catecholamine. To distinguish between these actions rats were given drugs before or after the intravenous injection of ^{3}H-noradrenaline and the amount of the ^{3}H-catecholamine in the heart was measured.

Male rats (Sprague–Dawley), weighing from 160–180 gm., received 10 μc./100 gm. *dl*-7-^{3}H-noradrenaline (20 mc./mgm.) in the tail vein. The rats were killed after 2, 4 or 24 hr., and the hearts were homogenized with 12 ml. of ice-cold 0·4 *N* perchloric acid. After centrifugation the supernatant solution was assayed for ^{3}H-noradrenaline[6]. Drugs were given before or after ^{3}H-noradrenaline as shown in Table 1. Rats were divided at random in groups of 6–12 for each drug treatment.

Reserpine, amphetamine, *d*-adrenaline and phenoxybenzamine reduced the amount of ^{3}H-noradrenaline in the heart when given after as well as before the ^{3}H-catecholamine (Table 1). Tyramine was previously shown to have this action[7]. It is concluded that these drugs release the bound hormone from its storage site. The experimental technique does not distinguish whether or not these drugs may also inhibit the uptake of ^{3}H-noradrenaline.

Table 1. EFFECT OF DRUGS ON THE UPTAKE AND RELEASE OF ^{3}H-NORADRENALINE IN RAT HEART

Drug	Dose (mgm./kgm.)	Time drug given before or after ^{3}H-noradrenaline	Time rats killed after ^{3}H-noradrenaline (hr.)	^{3}H-Noradrenaline in heart (mμc./gm.)
None	—	—	2	300 ± 15
Chlorpromazine	10	30 min. before	2	112 ± 6 *
Chlorpromazine	10	30 min. after	2	271 ± 14
None	—	—	24	58 ± 9
Chlorpromazine	10, 10	30 min. and 12 hr. after	24	49 ± 10
None	—	—	2	276 ± 15
Imipramine	10	30 min. before	2	132 ± 8 *
Imipramine	10	30 min. after	2	269 ± 25
None	—	—	24	91 ± 11
Imipramine	10, 10	30 min and 12 hr. after	24	94 ± 12
None	—	—	4	216 ± 17
Reserpine	1	30 min. before	4	3 ± 0·5 *
Reserpine	1	30 min. after	4	17 ± 2 *
None	—	—	2	240 ± 28
d-Adrenaline	2	10 min. before	2	115 ± 5 †
d-Adrenaline	2	0·5 min. before	2	99 ± 5 *
d-Adrenaline	2	10 min. after	2	159 ± 22 ‡
None	—	—	4	217 ± 15
Phenoxybenzamine	20	30 min. before	4	111 ± 17 *
Phenoxybenzamine	20	30 min. after	4	119 ± 21 †
None	—	—	4	217 ± 15
Dichloriso-proterenol	20	30 min. before	4	148 ± 11 †
Dichloriso-proterenol	20	30 min. after	4	173 ± 19
None	—	—	4	268 ± 7
Amphetamine	5	30 min. before	4	44 ± 10 *
Amphetamine	5	30 min. after	4	164 ± 14 *

All drugs were given intramuscularly except *d*-adrenaline, which was given intravenously. Twelve animals were used for phenoxybenzamine and dichlorisoproterenol and six for all other drugs.
* $P < 0.001$. † $P < 0.01$. ‡ $P < 0.05$.

Treatment with chlorpromazine, imipramine and dichlorisoproterenol produced a lower concentration of ^{3}H-noradrenaline when given before, but not after, the ^{3}H-catecholamine (Table 1). Cocaine was previously shown to have this action[7]. From these observations, it appears that these drugs block the entry of ^{3}H-noradrenaline into storage sites but do not cause its release.

Because chlorpromazine and imipramine blocked the uptake of ^{3}H-noradrenaline, the ability of these drugs to block its release was examined. Previous studies have shown that monoamine oxidase inhibitors produce a higher concentration of ^{3}H-noradrenaline in the rat after 24 hr. by preventing the spontaneous release of the hormone[8]. Chlorpromazine and imipramine did not appear to block the release of ^{3}H-noradrenaline in 24 hr. (Table 1).

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